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Docket No: 50370-60623 CIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	James R. Broach, *et al.*	
Application No.:	09/581,861	Group No.: 1639
Filed:	June 19, 2000	Examiner: Celsa, Bennett M.
For:	*YEAST CELLS EXPRESSING MODIFIED G PROTEINS AND METHODS OF USE THEREFOR*	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being facsimile transmitted to Group No. 1639 at 703-872-9306 of the United States Patent and Trademark Office on August 20, 2004.

PETER C. LAURO
Name of Person Signing

Peter C. Lauro
Signature

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RESPONSE TO RESTRICTION REQUIREMENT

Dear Sir:

This document is submitted in response to the Office Action mailed from the United States Patent and Trademark Office on July 21, 2004.

REMARKS

Claims 1-61 and 109-119 are pending in the instant application, and are subject to restriction.

The Office Action, on page 2, requires restriction to one of the following groups under 35 U.S.C. §121 and 372:

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Group 1, claim(s) 1(in part), 4, 6-8 and 26, drawn to recombinant yeast comprising a heterologous G protein coupled receptor (GPCR) and substituted heterologous G protein subunit.

Group 2, claim(s) 1(in part), 5, 9-25, drawn to recombinant yeast comprising heterologous GPCR and chimera of STE18 and heterologous G (gamma) subunit.

Group 3, claim(s) 1(in part), 2 (in part), 3, 44-61, drawn to recombinant yeast comprising heterologous GPCR and chimera of GPA1 (≤ 4 c-terminal substituted with heterologous G protein subunit amino acids) and optionally linked to at least the 1st five amino acids of a 2nd heterologous G protein subunit.

Group 4, claim(s) 27 and 28, drawn to an assay for identifying modulators of G (alpha) and G (beta-gamma) dissociation.

Group 5, claim(s) 29-43, drawn to an assay for identifying modulators of heterologous GPCR.

Groups 6-16, claim(s) 109-119, drawn to peptides comprising sequences 107-115, 118 and 123, respectively.

Applicants are required to elect one of the above groups for prosecution on the merits. Applicants respectfully traverse the requirements for restriction and election, and submit that the requirements are improper.

First, Applicants assert that the subject matter of these groups represent different embodiments of a single inventive concept for which a single patent should issue. The pending claims represent an intricate web of knowledge, continuity of effort, and consequences of a single invention, which merit examination of all of these claims in a single application. The unifying concept of the claimed invention is the coupling of a heterologous G protein-coupled receptor (GPCR) to yeast signaling pathways via non-natural G protein subunits, *i.e.*, chimeric and/or mutant G protein subunits.

The Examiner asserts that Groups 1-3 do not share a common special technical feature because recombinant yeast cells comprising fusions between heterologous G protein-coupled receptors (GCPR) and chimeric G protein subunits (e.g., yeast/mammals) are known in the art based on the disclosures of U.S. Patent 5,482,835 to King *et al.* ("the King patent") and Kang (1990 Mol. Cell. Biol. 10:2582-2590) ("the Kang reference"). Applicants respectfully disagree.

Neither the King patent nor the Kang reference contains a specific disclosure of any of the four members of the Markush group of claim 1 presented herein. The King patent discloses transformed yeast cells containing a first heterologous DNA sequence coding for a heterologous mammalian G protein-coupled receptor and a second heterologous DNA sequence coding for a mammalian Gα protein subunit. There is no teaching or suggestion in the King patent of a chimeric G protein subunit defined by the Markush group recited in claim 1 presented above. Rather, the King patent exemplifies replacement of the complete endogenous yeast Gα subunit with a complete, but otherwise naturally occurring mammalian Gα subunit.

The Kang reference discusses the effects of mammalian Gα and hybrid mammalian yeast Gα proteins on the yeast pheromone response signal transduction pathway. In particular, the Kang reference describes recombinant yeast cells in which the endogenous yeast Gα subunit was either replaced in its entirety with mammalian Gα subunits, or a portion of the endogenous yeast Gα was replaced with a portion of a mammalian Gα subunit. In all cases, the effects of these changes to the pheromone response pathway were studied in yeast cells having the endogenous yeast pheromone receptors Mata and Matα that are specific for a-factor and α-factor, respectively. Contrary to the recitation of claim 1, there is no teaching or suggestion in the Kang reference of a yeast cell engineered to express a heterologous G protein-coupled receptor that acts as a surrogate for an endogenous yeast pheromone receptor. D1 discloses only yeast cells having the endogenous Matα and Mata G protein-coupled receptors.

The authors of the Kang reference found that although the Gα constructs described in the reference were able to complement the endogenous Gα protein subunit (Scg1) by interacting with the βγ subunit to prevent activation of the pheromone pathway, the data suggest that these constructs are unable to interact with the pheromone receptors to activate the pathway. *See* Abstract. Because Applicants' invention relies on the ability of the claimed chimeric G protein subunits to functionally couple to the heterologous receptor and activate the pheromone pathway, the foregoing statement in the Abstract of the Kang reference constitutes a clear teaching away from the claimed invention.

Notwithstanding the foregoing, Applicants submit that a sufficient search and examination with respect to the subject matter of all claims can be made without serious burden. As the M.P.E.P. states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

M.P.E.P. § 803 (8th ed., August 2001).

That is, even if the above-enumerated groups of claims are drawn to distinct inventions, the Examiner must still examine the entire application on the merits because doing so will not result in a serious burden.

Applicants submit that the search and examination of all the claims will have substantial overlap, and no serious burden will result from searching and examining all claims in the same application.

Therefore, in the interest of savings of time and cost to Applicants and the Patent Office, Applicants respectfully request that all the claims be searched and examined in a single application and that all groups be rejoined into a single group.

Nevertheless, in compliance with the directives in the Office Action and in order to expedite prosecution of the instant application, Applicants hereby provisionally elect, subject to the foregoing traverse, Group 3, claims 1(in part), 2 (in part), 3, 44-61, drawn to recombinant yeast comprising a heterologous GPCR and an endogenous yeast Gpa1 subunit in which at least the last four C-terminal amino acids of the Gpa1 are replaced with at least the last four C-terminal amino acids of a first heterologous G protein subunit, and in which the N-terminus of the Gpa1 is operably linked to at least the first five N-terminal amino acids of a second heterologous G protein subunit, wherein said first and second heterologous G protein subunits are the same or different.

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The Examiner further requires election of a single disclosed species within the context of the above election of Group 3. Accordingly, Applicants provisionally elect the human bradykinin receptor as the heterologous G protein coupled receptor and the sandwich chimera Gαq(1-11)-GPA1(6-467)-Gαq(355-359) of Example 12 in the specification.

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 439-4444.

Respectfully submitted,

Date: August 20, 2004

By

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